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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

T. FURUZONO et al.

Any. Ref.: 1035-530; Confirmation No. 6831

Appl. No. 10/510,132

TC/A.U. 1775

Filed: October 4, 2004

Examiner: Daniel H. Miller

For: TITANIUM OXIDE COMPLEX AND PRODUCTION METHOD THEREOF, AND
MEDICAL MATERIAL USING THE SAME.

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Commissioner for Patents :
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF DR. TSUTOMU FURUZONO

Dr Tsutomu Furuzono of 5-7-1 Aoyamadaei Suita-shi, Osaka, 565-0875, Japan, hereby
declares as follows:

1. For the last eight years, I have been employed by the assignee of the above-
identified application, National Cardiovascular Center as Division Head in the Department of
Bioengineering, and graduated from the Graduate School of Kagoshima University in 1996 with
a degree in Dr. of Engineering

2. I am a joint inventor of the subject matter in the above-identified patent
application.

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3. The above-identified patent application is directed to a new and improved titanium oxide complex, comprising a polymer-based material having an active group; and titanium oxide having a reactive functional group which is capable of reacting with the active group, wherein the active group and the reactive functional group are bonded directly to each other based on a chemical bond, and the reactive functional group is an amino group, and the chemical bond is an amido bond.

4. The above-identified patent application is also directed to a new and improved titanium oxide complex comprising a hydroxyl group contained in titanium oxide; and a polymer-based material having a functional group which is capable of chemically bonding to the hydroxyl group, wherein the hydroxyl group and the polymer-based material are bonded directly to each other based on a chemical bond, and the functional group is an alkoxysilyl group.

5. In the titanium oxide complex of the present invention, the titanium oxide is firmly bonded to the surface of a polymer-based material without impairing the original properties of the titanium oxide and the polymer-based material. The titanium oxide complex is an excellent material having both an antimicrobial property derived from photocatalyst activity and high adhesiveness to tissues.

6. The high adhesiveness to tissues is realized by an amino group on the surface of the titanium oxide. Fig. 1 annexed hereto is a graph showing the relationship between the amount of an amino group introduced to the titanium oxide and the adhesiveness of cells. It is noted that Fig. 1 confirms that the number of adhering cells increases as the number of an amino group introduced to the titanium oxide increases. This result indicates that high adhesiveness to tissues is realized by an amino group on the surface of the titanium oxide.

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7. The data in Fig. 1 annexed hereto was obtained in accordance with the method used in the cell adhesion test in the Examples in the specification of the above-identified patent application. The specific method is as follows:

(i) Sheets (1.5 cm in diameter) of a titanium oxide complex of the present invention, each with different amounts of introduced amino groups, were stillly placed on a 24-Multiwall®, 1x10⁵ mice fibroblasts (L929 cells) were inoculated, and cultivated at 37°C for 24 hours.

(ii) The sheets were taken out and rinsed with phosphate buffer three times.

(iii) The number of adhering cells was obtained by observing the rinsed sheets with use of a scanning electronic microscope and counting the number of cells seen in photographs of the observation.

8. The Examiner has cited the following references against the claims of the above-identified patent application which recite the titanium oxide complex set forth in paragraphs 3 and 4 hereof:

Stokes (U.S. 6968234)

Gagliardi (U.S. 3547688)

Lomas (U.S. 6716908)

Furuya et al. (U.S. 6048910)

JP 4021095 70A

JP 2002311028

None of the above-listed references cited by the Examiner, taken individually or in combination, discloses or even suggests a titanium oxide complex obtained through an amide bond between titanium oxide having an amino group and a polymer-based material having a reactive functional group, as more specifically described in paragraphs 3 and 4 hereof and recited

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in claims 1, 3-5, 6, 8 and 9 of the present application. Accordingly, none of the compositions or complexes disclosed in the above-listed references is capable of achieving the high adhesiveness to tissues realized by the amino group on the surface of the titanium oxide of the complex of the present invention, as demonstrated in Fig. 1 annexed hereto.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 101 of Title 18 of the U.S. code and that such willful false statements may jeopardize the validity of the above-identified application or any patent issued thereon.

Date: Sep. 5, 2008

古蘭 勉
Dr. Tsutomu Furuzono

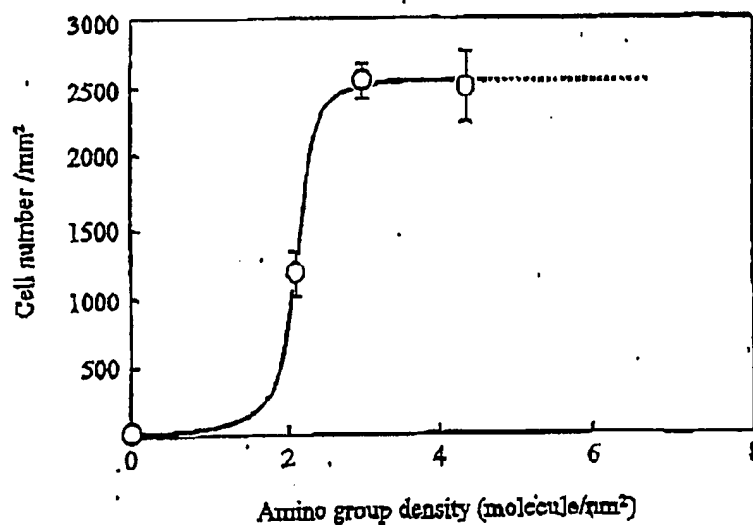


Fig. 1 Relationship between the amino group density on the TiO_2 particle surfaces and the number of L929 cells adhering on the TiO_2 /silicone composite sheets after incubation in 24-well multiplates (1×10^5 cells/well) at 37°C for 24 h.